Remarks

The Office Action Summary on page 1 of the office action is inconsistent with the Detailed Action. Claims 1-14 are under examination according to the Detailed Action. Claims 1-9 of Group I claims were rejoined with the Group II claims. However, inexplicably, claims 23 and 24 which were part of Group I and which are dependent on claim 6, which is dependent on claim 1, were not rejoined. It is respectfully submitted that these claims should form part of the same invention as claims 1 and 6 from which they depend.

The Rejection of Claims 11-14 under 35 U.S.C. § 112, second paragraph

Claims 11-14 are rejected as indefinite because the gene designation BRAF is used without a sequence identifier. "BRAF," contrary to the assertion of the office action, is not a mere laboratory designation. It is the name of the gene as it is used in the relevant art. Nonetheless, a sequence identifier has been added to the claim to clarify the meaning of the nucleotide number recited in claim 11.

Withdrawal of this rejection is respectfully requested.

The Rejection of Claims 1-14 under 35 U.S.C. § 112, first paragraph

Claims 1-14 are stated as rejected as not enabled in the specification for their full scope. However, the discussion for the reasons for the rejection seems to pertain only to claims 10 and 11-14. See page 4, first paragraph of the Office Action, paper no. 20060103. This rejection is respectfully traversed.

The Office Action asserts that "one [of ordinary skill in the art] cannot determine that the claimed methods would be useful in distinguishing benign thyroid neoplasms from malignant thyroid neoplasms." Office Action at page 4, lines 18-20. The PTO explains that the T →A transversion at nucleotide 1796 of *BRAF* has been found in a high percentage of malignant melanomas and colon carcinomas, as well as being found in head and neck cancers and in lung cancers. Therefore, the PTO reasons, a test in a blood sample would not permit determination of a malignant thyroid neoplasm because other types of cancers could be causing the detectable mutation in the blood. Moreover, even a neoplasm in the thyroid may not be a thyroid cancer, the PTO reasons, malignant melanoma is known to metastasize to the thyroid.

Claim 10 has been amended to recite that the human [whose blood is being tested] is suspected of having a thyroid neoplasm. Thus, if testing blood of a person who is suspected of having a thyroid neoplasm, the result is ***likely*** to be relevant to the thyroid neoplasm (not to a second tumor in another part of the body, the likelihood of two tumors being the product of the likelihood of each individual tumor. Moreover, the result is not likely to be related to a melanoma metastasis to the thyroid because those are very rare. "Clinically significant [melanoma] metastases to the thyroid gland are very rare. " Bozbara et al., "Thyroid metastasis of malignant melanoma," December 2005; Am. J. Clin. Oncol. 28:642-3; abstract enclosed.

No diagnostic or prognostic test is 100% accurate, and the PTO does not require 100% accuracy for enablement of a diagnostic or prognostic method. The standard for enablement permits a reasonable number of inoperatives, *i.e.,* false positive results. Thus it is respectfully submitted that the mere possibility that the blood test would detect a rare second tumor or a very rare melanoma metastasis to the thyroid does not render the claimed method not enabled. Withdrawal of this rejection with respect to claim 10 is therefore requested.

With regard to claims 11-14, the recited methods do not specify anything about blood or about thyroid malignancies, or about conclusions of diagnosis or prognosis. Thus the reasoning of the rejection does not apply to these claims.

With regard to claims 1-9, the recited methods specify testing of a "thyroid sample of a human." Thus the reasoning of the rejection (regarding blood test interpretation) does not apply to these claims. The concern regarding malignant melanoma metastases to the thyroid may have been intended to apply to these claims. However, as already discussed above, such metastases are "very rare" and enablement does not require 100% accuracy.

Withdrawal of this rejection as it applies to all of claims 1-14 is respectfully requested for the reasons detailed above.

Claims 11-14 are separately rejected because the method does not specify that it is for detecting a T →A transversion. Claim 11 has been amended to specify the transversion, rendering this portion of the rejection moot.

The Rejection of Claims 11-14 under 35 U.S.C. § 112, first paragraph

Claims 11-14 are rejected as not supported by an adequate written description for

mutation other than the T →A transversion. Claim 11 has been amended to recite this mutation, rendering the rejection moot.

A speedy allowance of all claims is respectfully requested.

Respectfully submitted,

Dated: July 11, 2006 ~~July 12, 2006~~

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Enclosure: Bozbora et al., abstract